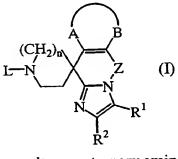
Claims

1. A compound of formula



(I)

a prodrug, a *N*-oxide, an addition salt, a quaternary amine or a stereochemically isomeric form thereof wherein

R^1 is hydrogen, C_{1-6}alkyl, halo, formyl, carboxyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkylcarbonyl, $N(R^3R^4)C(=O)$-, $N(R^3R^4)C(=O)N(R^5)$-, ethenyl substituted with carboxyl or C_{1-6}alkyloxycarbonyl, or C_{1-6}alkyl substituted with hydroxy, carboxyl, C_{1-6}alkyloxy, C_{1-6}alkyloxycarbonyl, $N(R^3R^4)C(=O)$-, C_{1-6}alkylC(=O)$N(R^5)$-, C_{1-6}alkylS(=O)$_2N(R^5)$- or $N(R^3R^4)C(=O)N(R^5)$-;

wherein each R^3 and each R^4 independently are hydrogen or C_{1-4}alkyl;

R^5 is hydrogen or hydroxy;

R^2 is hydrogen, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, C_{1-6}alkyloxyC_{1-6}alkyl, $N(R^3R^4)C(=O)$-, aryl or halo;

n is 1 or 2;

-A-B- represents a bivalent radical of formula

-Y-CH=CH- (a-1);

-CH=CH-Y- (a-2); or

-CH=CH-CH=CH- (a-3);

wherein each hydrogen atom in the radicals (a-1) to (a-3) may independently be replaced by R^6 wherein R^6 is selected from C_{1-6}alkyl, halo, hydroxy, C_{1-6}alkyloxy, ethenyl substituted with carboxyl or C_{1-6}alkyloxycarbonyl, hydroxyC_{1-6}alkyl, formyl, carboxyl and hydroxycarbonylC_{1-6}alkyl;

each Y independently is a bivalent radical of formula -O-, -S- or $-NR^7$-;

wherein R^7 is hydrogen, C_{1-6}alkyl or C_{1-6}alkylcarbonyl;

Z is a bivalent radical of formula

$-(CH_2)_p$- (b-1),

-CH=CH- (b-2),

$-CH_2$-CHOH- (b-3),

$-CH_2$-O- (b-4),

$-CH_2$-C(=O)- (b-5), or

$-CH_2$-C(=NOH)- (b-6),

provided that the bivalent radicals (b-3), (b-4), (b-5) and (b-6) are connected to the nitrogen of the imidazole ring via their -CH_2- moiety;

wherein p is 1, 2, 3 or 4;

L is hydrogen; C_{1-6}alkyl; C_{2-6}alkenyl; C_{1-6}alkylcarbonyl; C_{1-6}alkyloxycarbonyl; C_{1-6}alkyl substituted with one or more substituents each independently selected from hydroxy, carboxyl, C_{1-6}alkyloxy, C_{1-6}alkyloxycarbonyl, aryl, aryloxy, cyano or R^8HN- wherein R^8 is hydrogen, C_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkylcarbonyl; or

L represents a radical of formula

-Alk-Y-Het^1 (c-1),

-Alk-NH-CO-Het^2 (c-2) or

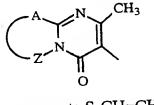
-Alk-Het^3 (c-3) ; wherein

Alk represents C_{1-4}alkanediyl ;

Y represents O, S or NH ;

Het^1, Het^2 and Het^3 each represent furanyl, tetrahydrofuranyl, thienyl, oxazolyl, thiazolyl or imidazolyl each optionally substituted with one or two C_{1-4}alkyl substituents; pyrrolyl or pyrazolyl optionally substituted with formyl, hydroxyC_{1-4}alkyl, hydroxycarbonyl, C_{1-4}alkyloxycarbonyl or with one or two C_{1-4}alkyl substituents; thiadiazolyl or oxadiazolyl optionally substituted with amino or C_{1-4}alkyl; pyridinyl, pyrimidinyl, pyrazinyl or pyridazinyl each optionally substituted with C_{1-4}alkyl, C_{1-4}alkyloxy, amino, hydroxy or halo; and

Het^3 may also represent 4,5-dihydro-5-oxo-1H-tetrazolyl substituted with C_{1-4}alkyl, 2-oxo-3-oxazolidinyl, 2,3-dihydro-2-oxo-1H-benzimidazol-1-yl or a radical of formula



wherein

A-Z represents S-CH=CH, S-CH_2-CH_2, S-CH_2-CH_2-CH_2, CH=CH-CH=CH, or CH_2-CH_2-CH_2-CH_2;

aryl is phenyl or phenyl substituted with 1, 2 or 3 substituents each independently selected from halo, hydroxy, C_{1-4}alkyl, polyhaloC_{1-4}alkyl, cyano, aminocarbonyl, C_{1-4}alkyloxy or polyhaloC_{1-4}alkyloxy;

provided that 5,6-dihydrospiro[imidazo[1,2-b][3]benzazepine-11[11*H*],4'-piperidine] and pharmaceutically acceptable addition salts thereof are not included.

2. A compound according to claim 1 wherein L is hydrogen, C_{1-6}alkyl, C_{1-6}alkylcarbonyl, C_{1-6}alkyloxycarbonyl or C_{1-6}alkyl substituted with hydroxy, carboxyl, C_{1-6}alkyloxy or C_{1-6}alkyloxycarbonyl.

3. A compound according to claim 1 wherein L is C_{1-6}alkyl substituted with aryl and C_{1-6}alkyloxycarbonyl.

4. A compound according to any one of the preceding claims wherein -A-B- is a bivalent radical of formula -CH=CH-CH=CH- (a-3) or –CH=CH-Y- (a-2).

5. A compound according to any one of the preceding claims wherein Z is $-(CH_2)_p-$ (b-1), -CH=CH- (b-2), or $-CH_2-O-$ (b-4).

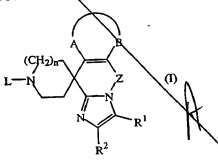
6. A compound according to claims 1, 2, 4 or 5 wherein L is hydrogen, C_{1-6}alkyl, hydroxyC_{1-6}alkyl, carboxyC_{1-6}alkyl, C_{1-6}alkyloxycarbonyl, or C_{1-6}alkyloxycarbonylC_{1-6}alkyl.

7. A compound according to any one of the preceding claims wherein R^1 is hydroxyC_{1-6}alkyl, formyl, C_{1-6}alkyloxycarbonyl, C_{1-6}alkyloxyC_{1-6}alkyl, $N(R^3R^4)C(=O)-$, halo or hydrogen.

8. A compound according to claim 1 wherein the compound is
5,6-dihydrospiro[11*H*-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-carboxamide dihydrochloride;
1'-butyl-5,6-dihydrospiro[imidazo[2,1-b] [3] benzazepine-11-[11*H*],4'-piperidine];
6,11-dihydro-1'-methylspiro[5*H*-imidazo[2,1-b][3]benzazepine-11,4'-piperidine] cyclohexylsulfamate(1:2);
6,11-dihydrospiro[5-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-methanol] (E)-2-butenedioate (2:1);
3-chloro-6,11-dihydrospiro[5*H*-imidazo[2,1-b][3]benzazepine-11,4'-piperidine] (E)-2-butenedioate (1:1);
6,11-dihydro-3-(methoxymethyl)spiro[5*H*-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]. (E)-2-butenedioate (1:1);
6,11-dihydro-1'-(2-hydroxyethyl)spiro[5*H*-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-carboxamide;
6,11-dihydro-1'-methylspiro[5*H*-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-3-carboxamide monohydrate;
ethyl 3-(aminocarbonyl)-6,11-dihydro-α-phenylspiro[5*H*-imidazo[2,1-b][3]-benzazepine-11,4'-piperidine]-1'-propanoate monohydrochloride;
3-(aminocarbonyl)-6,11-dihydrospiro[5*H*-imidazo[2,1-b][3]-benzazepine-11,4'-piperidine]-1'-carboxylate;

spiro[10*H*-imidazo[1,2-a]thieno[3,2-d]azepine-10,4'-piperidine];
6,11-dihydrospiro[5*H*-imidazo[2,1-b][3]benzazepine-11,4'-piperidine]-2,3-dicarboxamide dihydrochloride monohydrate;
a prodrug, a *N*-oxide, an addition salt, a quaternary amine or a stereochemically isomeric form thereof.

9. A compound of formula



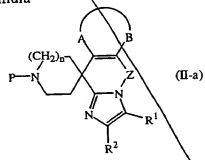
(I)

a prodrug, a *N*-oxide, an addition salt, a quaternary amine or a stereochemically isomeric form thereof wherein L, n, -A-B-, Z, R^1 and R^2 are defined as in claim1 for use as a medicine.

10. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, and as active ingredient a therapeutically effective amount of a compound as described in any one of claims 1 to 9.

11. A process of preparing a composition as claimed in claim 10, characterized in that, a pharmaceutically acceptable carrier is intimately mixed with a therapeutically effective amount of a compound as described in any one claims 1 to 9.

12. A compound of formula



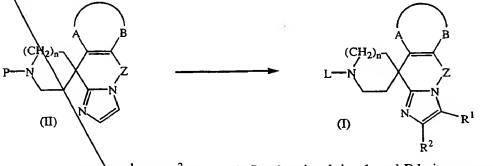
(II-a)

a *N*-oxide, an addition salt, a quaternary amine or a stereochemically isomeric form thereof wherein P is a protective group and n, -A-B-, Z, R^1 and R^2 are defined as in claim 1, provided that 6,11-dihydro-1'-(phenylmethyl)-5*H*-spiro[imidazo[1,2-b][3]-benzazepine-11,4'-piperidine] (E)-2-butenedioate(1:2) is not included .

13. A compound according to claim 12 wherein P is benzyl.

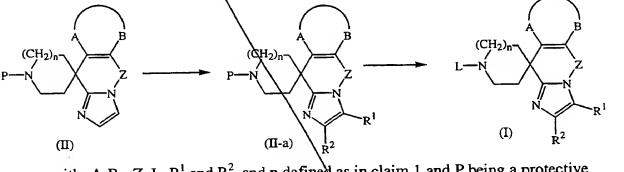
14. A process of preparing a compound as claimed in claim 1, characterized by,

a) deprotecting an intermediate of formula (II), followed optionally by derivatizing either the piperidine moiety, or the imidazole moiety, or both the piperidine moiety and the imidazole moiety



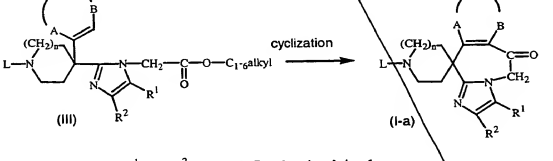
with -A-B-, Z, L, R^1 and R^2, and n defined as in claim 1 and P being a protective group;

b) derivatizing an intermediate of formula (II) at the imidazole moiety, leading to the formation of an intermediate of formula (II-a), followed by deprotecting the piperidine moiety, and followed optionally by derivatizing the piperidine moiety



with -A-B-, Z, L, R^1 and R^2, and n defined as in claim 1 and P being a protective group;

c) by cyclizing an intermediate of formula (III) in the presence of an appropriate acid, resulting in a compound of formula (I-a)

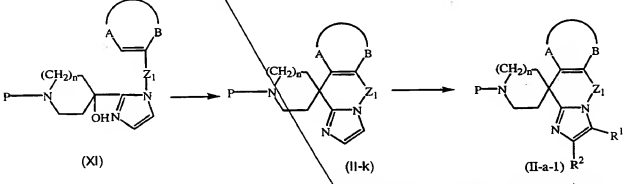


with -A-B-, L, R^1 and R^2, and n defined as in claim 1;

and, if desired, converting compounds of formula (I) and (I-a) into each other following art-known transformations, and further, if desired, converting the compounds of formula (I), into a therapeutically active non-toxic acid addition salt by treatment with an acid, or into a therapeutically active non-toxic base addition salt by treatment with a base, or conversely, converting the acid addition salt form into the free base by treatment with alkali, or converting the base addition salt into the free acid by treatment with acid; and, if desired, preparing stereochemically isomeric forms or N-oxide forms thereof.

15. A process of preparing a compound as claimed in claim 12, characterized by,

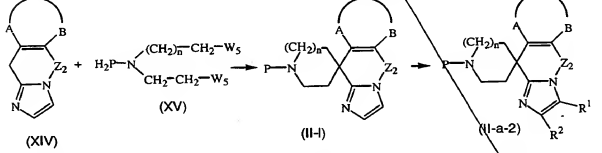
a) cyclizing a compound of formula (XI) with an appropriate acid, leading to a compound of formula (II-k), followed optionally by derivatizing the imidazole moiety, leading to a compound of formula (II-a-1)



(XI) (II-k) (II-a-1)

with -A-B-, R^1, R^2, n and P defined as in claim 13, and Z_1 being a bivalent radical of formula $-(CH_2)_p-$, wherein p is 1,2,3 or 4.

b) by reacting a tricyclic moiety of formula (XIV) with a reagent of formula (XV) under an inert atmosphere in a reaction inert solvent in the presence of a suitable base, leading the a compound of formula (II-l), followed optionally by derivatizing the imidazole moiety leading to a compound of formula (II-a-2)



(XIV) (XV) (II-l) (II-a-2)

with -A-B-, R^1, R^2, n and P defined as in claim 13, W_5 being a suitable leaving group, e.g. a halo, and Z_2 being a bivalent radical of formula $-(CH_2)_p-$, or $-CH_2-O-$, wherein p is 1,2,3 or 4.